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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/738,599	12/15/2000	Lisa K. Nolan	255.0001 0122	1240

26813 7590 07/30/2004

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/738,599	NOLAN ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-33,37-45 and 67-70* is/are pending in the application.

4a) Of the above claim(s) *35,36 and 46-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32,37-45,67,68 and 70* is/are rejected.

7)☒ Claim(s) *30,33 and 69* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence search report (1)*.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 04/27/04 in response to the non-final Office Action mailed 01/27/04.

Status of Claims

2) Claims 32, 45and 67 have been amended via the amendment filed 04/27/04.

Claims 30-33 and 35-70 are pending.

Claims 30-33, 37-45 and 67-70 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

5) The rejection of claim 32 made in paragraph 12(a) of the Office Action mailed 01/27/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

6) The rejection of claim 45 made in paragraph 12(b) of the Office Action mailed 01/27/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

7) The rejection of claim 67 made in paragraph 12(c) of the Office Action mailed 04/18/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

8) The rejection of claims 37-40, 43 and 67 made in paragraph 13 of the Office Action mailed 04/18/03 under 35 U.S.C § 102(b) as being anticipated by Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982, Applicants' IDS), is withdrawn. Applicants' main argument that Sanger *et al.* do not teach that the polypeptide is expressed has been noted. A prior art which teaches that the

polypeptide is expressed in applied below to reject the claims.

9) The rejection of claims 37 and 41 made in paragraph 14 of the Office Action mailed 04/18/03 under 35 U.S.C § 103(a) as being unpatentable over Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982 - Applicants' IDS) in view of Applicants' admitted state of the prior art, is withdrawn. Applicants' main argument that Sanger *et al.* do not teach that the polypeptide is expressed has been noted. A prior art which teaches that the polypeptide is expressed in applied below to reject the claims.

10) The rejection of claim 42 made in paragraph 15 of the Office Action mailed 04/18/03 under 35 U.S.C § 103(a) as being unpatentable over Sanger *et al.* (*J. Mol. Biol.* 162: 729-773, 1982 - Applicants' IDS) and Krieg *et al.* (WO 96/02555), is withdrawn.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

11) Claims 43 and 70 and claims 45 and 67 dependent therefrom are rejected under 35 U.S.C § 112, first paragraph, as being as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 43 and 70 include the limitations: the nucleic acid molecule .....'or an immunogenic subunit or immunogenic fragment thereof'. This immunogenic subunit and immunogenic fragment is of the nucleic acid molecule comprising nucleotides 73 to 309 of the nucleotide sequence of SEQ ID NO: 22. However, there is no descriptive support for an 'immunogenic subunit' or 'immunogenic fragment' of the nucleic acid molecule in the instant specification, as originally filed. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claims, or to point to specific pages and line numbers in the originally filed specification where support for such recitations can be found.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

12) Claims 31, 32, 37-45, 67 and 70 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 43 and 70 are confusing. The claim is directed a composition comprising nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22, or 'an immunogenic subunit or immunogenic fragment thereof'. It is unclear how much of the nucleic acid molecule's original structure has to be retained such that the nucleic molecule qualifies as an 'immunogenic subunit' or 'immunogenic fragment thereof'. It is further unclear how a 'subunit' or 'fragment' of a nucleic acid molecule can be 'immunogenic'. Does it mean that this 'subunit' or 'fragment' of the nucleic acid molecule elicits anti-nucleic acid molecule antibodies?

(b) Claim 37 is confusing in the recitation: 'an immunogenic fragment or immunogenic subunit thereof'. The active element in the claimed composition is an isolated nucleic acid molecule, which encodes a polypeptide. It is unclear whether the recited 'an immunogenic fragment or immunogenic subunit thereof' is a subunit or fragment of the claimed nucleic acid molecule, or a subunit or fragment of the polypeptide encoded by the nucleic acid molecule.

(c) Analogous criticism applies to claim 68.

(d) Claims 31 and 32 lack antecedent basis in the limitation: 'nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22'. Claims 31 and 32 depend from claim 30, which already includes the limitation: 'nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22'. For proper antecedence, it is suggested that Applicants replace the limitation with, --the nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22--.

(e) Claim 45 lacks antecedent basis in the limitation: 'nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22'. Claim 45 depends from claim 43, which already includes the limitation: 'nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22'. For proper antecedence, it is suggested that Applicants replace the limitation with, --the nucleotides 73 to 309 of the nucleotide sequence SEQ ID NO: 22--.

(f) Claims 38-45 and claim 67, which depend directly or indirectly from claim 37, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

13) Claims 37-40, 43, 67 and 68 are rejected under 35 U.S.C § 102(b) as being anticipated by Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess, 1990) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988, already of record).

Barondess *et al.* (1990) disclosed an isolated nucleic acid molecule comprising several long stretches of nucleotides showing 100% sequence identity with nucleotides 73 to 309 of SEQ ID NO: 22, plasmids, vectors, phages, and host cells comprising the same. See the attached sequence search report and Figure 1 of Barondess *et al.* (1990). Barondess *et al.* (1990) taught an isolated *bor* gene sequence which encodes an envelope protein, gene fusions, fragments thereof, and fusions expressed in lysogens (see pages 871 and 872; and Fig 1 and Figure 1 legend). The fusion fragments were subcloned and sequenced. The cells expressing the polypeptide are contained in PBS (i.e., a pharmaceutically acceptable carrier). The products are contained in PBS, i.e., a pharmaceutically acceptable carrier (see page 873). The long fragments of Barondess' nucleic acid molecule are expected to encode a fragment of a polypeptide that is long enough to serve as an immunogenic fragment or immunogenic subunit. For instance, the polypeptide fragment or subunit encoded by Barondess' nucleotide sequence encoding the polypeptide fragment or subunit, KTVDAAKICGGAENVVKTETQQTFVNGLLGFIT, is long enough to be immunogenic, given the art-known fact that a polypeptide fragment of a full length protein that is at least 6 amino acid-long is long enough to be immunogenic to induce an antibody response in a subject (see page 76 of Harlow *et al.*). The fact that Barondess' polypeptide fragment or subunit was expressed or encoded indicates that Barondes' nucleic acid molecule further comprises a regulatory sequence or a control sequence operably linked to the nucleotide sequence. Furthermore, Barondess' PBS-suspended bacterial host cells comprising the above-identified nucleotide sequence inherently serve as immunogenic compositions.

The teachings of Barondess *et al.* (1990) anticipate the instant claims. Harlow *et al.* is **not** used as a secondary reference in combination with Barondess *et al.* (1990), but rather is used to show that every element of the claimed subject matter is disclosed by Barondess *et al.* (1990) with the unrecited limitation(s) being inherent in view of what is well known in the art as explained

above. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Claims 37-40, 43, 67 and 68 are anticipated by Barondess *et al.* (1990).

14) Claims 37 and 41 are rejected under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) in view of Applicants' admitted state of the prior art.

Claim 37 is included in this rejection since claim 41 includes the limitation 'claim 37'.

The teachings of Barondess *et al.* (1990) are explained above which do not expressly disclose that the regulatory or control sequence causes expression of the polypeptide in an animal cell.

However, the expression of an art-known nucleic acid molecule via an art-known regulatory or control sequence that causes expression in an animal cell line was routine and conventional in the art at the time of the invention. For instance, Applicants acknowledge in the instant specification the following to be known in the art: transformation and transfection methods; a wide variety of control or promoter sequences, compatible vectors, and eukaryotic expression systems or cell lines known to those skilled in the art of molecular biology to express polynucleotides; the use of vaccinia recombinant plasmid; the production of fusion protein for easy purification; and the standard affinity chromatography and purification methods. See pages 28-34 of the specification.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Barondess' (1990) nucleic acid molecule or polynucleotide via any one of the admittedly art-known animal or mammalian cell using any one of the admittedly art-known compatible control or regulatory sequences suing art known techniques to produce the instant invention, with a reasonable expectation of success. Expression of Barondess' DNA via an animal cell is well within the realm of routine experimentation. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of improved expression of Barondess' polynucleotide since improved expression is ideally desired in the art.

Claims 37 and 41 are *prima facie* obvious over the prior art of record.

15) Claim 42 is rejected under 35 U.S.C § 103(a) as being unpatentable over Barondess *et al.* (*Nature* 344: 871-874, 1990, already of record) (Barondess *et al.*, 1990) and Krieg *et al.* (WO

96/02555, already of record).

The teachings of Barondess *et al.* (1990) are explained above, which do not disclose the their polynucleotide further comprising an immunostimulatory sequence.

However, the use of immunostimulatory sequences, for example, an immunostimulatory oligonucleotide sequence along with a heterologous polynucleotide sequence for the purpose of immunostimulation was well known in the art at the time of the invention. For instance, Krieg *et al.* showed that it was routine and conventional in the art to use a CpG immunostimulatory nucleotide sequence in a pharmaceutical composition (see abstract; and claims).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to express Barondess' (1990) nucleic acid molecule together with Krieg's immunostimulatory oligonucleotide sequence to produce the instant invention with a reasonable expectation of success. Given Krieg's teaching of the routine and conventional nature of using an immunostimulatory oligonucleotide in a pharmaceutical composition for the purpose of immunostimulation, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immune response to Barondess' (1990) product.

Claim 42 is *prima facie* obvious over the prior art of record.

Remarks

16) Claims 31, 32, 37-45, 67, 68 and 70 stand rejected. Claims 30, 33 and 69 contain allowable subject matter.

In claims 30-33, 43-45, 69 and 70, for clarity, it is suggested that Applicants replace the limitation 'nucleotide sequence SEQ ID NO: 22' with --nucleotide sequence of SEQ ID NO: 22--. Similar amendment is suggested to the limitation 'sequence SEQ ID NO: 21' in claim 45.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

18) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER

ALIGNMENTS

73-309 of SEQ ID NO:22

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RESULT 1
BOR_LAMBD
ID   BOR_LAMBD      STANDARD;      PRT;    97 AA.
AC   P26814;
DT   01-AUG-1992 (Rel. 23, Created)
DT   01-AUG-1992 (Rel. 23, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Bor lipoprotein precursor.
GN   BOR.
OS   Bacteriophage lambda.
OC   Viruses; dsDNA viruses, no RNA stage; Caudovirales; Siphoviridae;
OC   Lambda-like viruses.
OX   NCBI_TaxID=10710;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=83189071; PubMed=6221115;
RA   Sanger F., Coulson A.R., Hong G.F., Hill D.F., Petersen G.B.;
RT   "Nucleotide sequence of bacteriophage lambda DNA.";
RL   J. Mol. Biol. 162:729-773(1982).
RN   [2]
RP   CHARACTERIZATION.
RX   MEDLINE=90363299; PubMed=2144037;
RA   Barondes J.J., Beckwith J.;
RT   "A bacterial virulence determinant encoded by lysogenic coliphage
RT   lambda.";
RL   Nature 346:871-874(1990).
CC   -!- FUNCTION: Not known; is expressed during lysogeny in Escherichia
CC       coli.
CC   -!- SUBCELLULAR LOCATION: Attached to the membrane by a lipid anchor
CC       (Probable).
CC   -!- SIMILARITY: TO PLASMID INCFI COLV2-K94 ISS PROTEIN.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X55792; CAA39317.1; -.
DR   InterPro; IPR000437; Prok_lipoprot_S.
DR   PROSITE; PS00013; PROKAR_LIPOPROTEIN; 1.
KW   Lipoprotein; Membrane; Signal; Palmitate.
FT   SIGNAL        1     16       POTENTIAL.
FT   CHAIN        17     97       BOR LIPOPROTEIN.
FT   LIPID        17     17       S-diacylglycerol cysteine (in host)
FT                                (Potential).
FT   LIPID        17     17       N-palmitoyl cysteine (in host)
FT                                (Potential).
SQ   SEQUENCE   97 AA;  10386 MW;  45CDAE2A5A48FF1E CRC64;

Alignment Scores:
Pred. No.:              8.97e-39        Length:         97
Score:                  381.00          Matches:        73
Percent Similarity:     94.87%          Conservative:   1
Best Local Similarity:  93.59%          Mismatches:     4
Query Match:            84.11%          Indels:         0
DB:                     1               Gaps:           0

US-09-738-599-22_COPY_73_309 (1-237) x BOR_LAMBD (1-97)

Qy          1 CAAACGTTTACTGTTGGAAACAAACCGACAGCAGTAACACCAAAGGAAACCATCACTCAT 60
              ||||||||||||||   |||||||||    ||||||   ||||||||||||||||||||
Db         20 GlnThrPheThrValGlnAsnLysProAlaAlaValAlaProLysGluThrIleThrHis 39

Qy         61 CATTTCTTCGTTTCGGGAATTGGACAAGAGAAAACTGTTGATGCAGCCAAAATTTGTGGC 120
              ||||||||||||||||||||||||||:::||||||||||||||||||||||||||||||
Db         40 HisPhePheValSerGlyIleGlyGlnLysLysThrValAspAlaAlaLysIleCysGly 59

Qy        121 GGTGCAGAAAATGTTGTTAAAACAGAAACTCAGCAAACATTCGTAAATGGATTGCTCGGT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         60 GlyAlaGluAsnValValLysThrGluThrGlnGlnThrPheValAsnGlyLeuLeuGly 79

Qy        181 TTTATCACTTTTGGCATCTATACTCCGCTGGAAGCCCGGGTATATTGCTCACAA 234
              |||||||||   ||||||||||||||||||||||||||||||||||||||||||
Db         80 PheIleThrLeuGlyIleTyrThrProLeuGluAlaArgValTyrCysSerGln 97
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